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14 September 2007

European Patent Office
Erhardtstraße 27
80469 München
Germany

Dear Sirs

European Patent Application No. 05706393.5
Lorus Therapeutics Inc
Our Ref: LAS01886EP

Please note our reference for this case is as above. I would be grateful if you would update the European Patent Register accordingly.

Yours faithfully
GILL JENNINGS & EVERY LLP

Elizabeth Swan

LAS/EMS/js

European Patent Office
80298 MUNICH
GERMANY
Tel.: +49 89 2399 - 0
Fax: +49 89 2399 - 4465

Europäisches Patentamt | European Patent Office | Office européen des brevets

Samuels, Lucy Alice
Gill Jennings & Every LLP
Broadgate House
7 Eldon Street
London EC2M 7LH
GRANDE BRETAGNE

EPO Customer Services
Tel.: +31 (0)70 340 45 00

Date: 07.08.07

Reference	Application No./Patent No.
	05706393.5 - 2406

Applicant/Proprietor: Lorus Therapeutics Inc.

Communication

concerning the registration of amendments relating to

☑ a transfer (Rules 20 and 61 EPC)

☐ entries pertaining to the applicant/the proprietor (Rule 92(1)(f) EPC)

As requested, the entries pertaining to the applicant of the above-mentioned European patent application / to the proprietor of the above-mentioned European patent have been amended to the following:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU MC NL PL PT RO SE SI SK TR
Lorus Therapeutics Inc.
2 Meridian Road
Toronto, Ontario M9W 4Z7/CA

The registration of the changes has taken effect on 18.07.07.

In the case of a published application/a patent, the change will be recorded in the Register of European Patents and published in the European Patent Bulletin (Section I.12/II.12).

Your attention is drawn to the fact that, in the case of the registration of a transfer, any automatic debit order only ceases to be effective from the date of its express revocation (cf. point 14(c) of the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 2/2002).

Transfer Service
Tel.: +49 (0)89 2399 2780

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17 July 2007

European Patent Office
Erhardtstraße 27
80469 München
Germany

EPO - Munich
23
19. Juli 2007

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www.gje.co.uk

Dear Sirs

European Patent Application No. 05706393.5
GeneSense Technologies Inc
Our Ref: LAS01886EP

This application has been assigned from GeneSense Technologies Inc. of 2 Meridian Road, Toronto, Ontario, M9W 4Z7 to Lorus Therapeutics Inc. of the same address. The assignment took place 10 July 2007. Please find enclosed an assignment document as evidence of this. The above identified application is shown at the bottom of page 4 of the document.

Please record the assignment on the European Patent Register. The fee for recording the assignment will be paid by separate communication.

Yours faithfully
GILL JENNINGS & EVERY LLP

Elizabeth Flexer

Enc

EMS/veh

ASSIGNMENT OF INVENTION

In consideration of One ($1.00) Dollar and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, we, **GENESENSE TECHNOLOGIES INC.** (hereinafter "the Assignor"), do hereby sell, assign and transfer to **LORUS THERAPEUTICS INC.** (hereinafter "the Assignee"), all our right, title and interest throughout the world in and to (1) the inventions relating to and described and/or claimed in the patent applications and patents listed in Schedule A; (2) all improvements, including but not limited to modifications, additions, substitutions, derivatives, and deletions to said invention(s); (3) the patent applications and patents listed in Schedule A and national phase applications thereof; (4) all other applications for Letters Patent in any country throughout the world for said invention(s) and improvements, including but not limited to all divisional, continuation, continuation-in-part, renewal, reissue, and substitute applications; (5) any Letters Patent which may issue from any of said applications as exemplified in (3) and (4) above in any country throughout the world; (6) all Convention or Treaty rights derived from any of said applications, including without limitation, all rights of priority throughout the world in and to said applications; and (7) the full and complete right to file applications for Letters Patent in the name of the Assignee, or in our name at the Assignee's election, on said invention(s) and improvements in all countries throughout the world.

For said consideration, the Assignor agrees, upon the request and at the expense of the Assignee, its successors and assigns, to execute any and all divisional, continuation, continuation-in-part, reissue and substitute applications for said invention(s) and improvements, and acknowledge and agree that all rights therein shall vest in the Assignee, its successors and assigns, whereby said Letters Patent will be held and enjoyed by said Assignee, its successors and assigns, to the full end of the term for which said Letters Patent will be granted, as fully and entirely as the same would have been held and enjoyed by the undersigned if this assignment had not been made. In addition, the Assignor will, at the request of the Assignee, execute any and all documents required by the Assignee to fully and properly vest the aforementioned rights in the Assignee.

The undersigned hereby grants to the firm of **MBM & CO.** whose full post office address is P.O. Box 809, Station B, Ottawa, Ontario, Canada, K1P 5P9, the power to insert on this assignment any further information and/or correct any clerical error in the information pertaining to the referenced applications and patents, which may be necessary or desirable in order to comply with the patent legislation for recordation of this document.

FOR THE ASSIGNOR:

SIGNED at Toronto, Ontario, Canada, this 10TH day of JULY, 2007.

Signature: Alice-G

Name: AIPING YOUNG

Title: PRESIDENT & CEO

GENESENSE TECHNOLOGIES INC.
2 Meridian Road, Toronto, Ontario M9W 4Z7, Canada

I was personally present and did see AIPING YOUNG duly sign and execute the above assignment.

(Signature of witness)

VANESSA GRANT
(Name of witness)

FOR THE ASSIGNEE:

SIGNED at Toronto, Ontario, Canada, this 10TH day of JULY, 2007.

Signature: Alice-G

Name: AIPING YOUNG

Title: PRESIDENT & CEO

LORUS THERAPEUTICS INC.
2 Meridian Road, Toronto, Ontario M9W 4Z7, Canada

I was personally present and did see AIPING YOUNG duly sign and execute the above assignment.

(Signature of witness)

VANESSA GRANT
(Name of witness)

Schedule A

ANTITUMOR ANTISENSE SEQUENCES DIRECTED AGAINST R1 AND R2 COMPONENTS OF RIBONUCLEOTIDE REDUCTASE
(GTI-2501)

Country	Filed	Serial #	Patent #
AUSTRALIA	2/9/2000	25292/00	780455
CANADA	2/9/2000	2,366,487	
EUROPE (Germany, Spain, France, Italy, Great Britain)	2/9/2000	903456.2	1153128
ISRAEL	2/9/2000	144727	
JAPAN	2/9/2000	2000-598831	
MEXICO	2/9/2000	2001/008137	
NEW ZEALAND	2/9/2000	514090	514090
UNITED STATES	2/11/1999	09/249,730	6,121,000
ARGENTINA	2/11/2000	P000100813	

ANTISENSE OLIGONUCLEOTIDES DIRECTED TO RIBONUCLEOTIDE REDUCTASE R1 AND USES THEREOF IN THE TREATMENT OF CANCER
(GTI-2501 in combination with chemotherapy)

Country	Filed	Serial #
CANADA	5/21/2004	2,526,393
EUROPE	5/21/2004	04734192.0
UNITED STATES	5/21/2004	10/557,853

ANTITUMOR ANTISENSE SEQUENCES DIRECTED AGAINST RIBONUCLEOTIDE REDUCTASE
(GTI-2040)

Country	Filed	Serial #	Patent #
UNITED STATES	8/1/1997	08/904,901	5,998,383

ANTITUMOR ANTISENSE SEQUENCES DIRECTED AGAINST R1 AND R2 COMPONENTS OF RIBONUCLEOTIDE REDUCTASE
(GTI-2040)

Country	Filed	Serial #	Patent #
AUSTRALIA	8/1/1997	38175/97	738592
CANADA	8/1/1997	2,262,776	2,262,776
CHINA	8/1/1997	97198163.9	97198163.9
EUROPE (Germany, Spain, France, Italy, Great Britain)	8/1/1997	97932690.7	917569
ISRAEL	8/1/1997	128124	
JAPAN	8/1/1997	10-507410	
NEW ZEALAND	8/1/1997	333802	333802
SINGAPORE	8/1/1997	9900413-7	61306
UNITED STATES	5/29/2003	10/447,138	

ANTISENSE OLIGONUCLEOTIDES DIRECTED TO RIBONUCLEOTIDE REDUCTASE R1 AND USES THEREOF IN THE TREATMENT OF CANCER
(GTI-2040 in combination with chemotherapy)

Country	Filed	Serial #
AUSTRALIA	2/10/2004	2004209579
CANADA	2/10/2004	2,535,650
EUROPE	2/10/2004	4709557.5
JAPAN	2/10/2004	2006-501413
UNITED STATES	2/10/2004	10/545,152

ANTISENSE OLIGONUCLEOTIDES DIRECTED TO RIBONUCLEOTIDE REDUCTASE R2 AND USES THEREOF IN COMBINATION THERAPIES FOR THE TREATMENT OF CANCER
(GTI-2040 in combination with cytokines)

Country	Filed	Serial #
AUSTRALIA	1/12/2005	2005203822
CANADA	1/12/2005	2,553,211
EUROPE	1/12/2005	5706393.5
JAPAN	1/12/2005	2006-548057
UNITED STATES	1/12/2005	10/585,772

OLIGONUCLEOTIDES FROM THE UNTRANSLATED REGIONS OF RIBONUCLEOTIDE REDUCTASE AND THEIR USE TO MODULATE CELL GROWTH
(U-sense)

Country	Filed	Serial #	Patent #
CANADA	6/30/1997	2,259,123	2,259,123

INHIBITING NEOPLASTIC CELLS UTILIZING THE RIBONUCLEOTIDE REDUCTASE UTR
(U-sense)

Country	Filed	Serial #
UNITED STATES	5/10/2002	09/214,388
UNITED STATES	8/8/2005	11/198,351

ANTITUMOR ANTISENSE SEQUENCES DIRECTED AGAINST R1 AND R2 COMPONENTS OF RIBONUCLEOTIDE REDUCTASE
(R1 antisense excluding GTI-2501)

Country	Filed	Serial #	Patent #
UNITED STATES	2/11/1999	09/249,247	6,593,305

SUPPRESSION OF MALIGNANCY UTILIZING RIBONUCLEOTIDE REDUCTASE R1
(R1 Gene Therapy)

Country	Filed	Serial #	Patent #
AUSTRALIA	3/18/1998	64922/98	742176
CANADA	3/18/1998	2,301,674	
EUROPE (Germany, Spain, France, Italy, Great Britain)	3/18/1998	98910553.1	971731
HONG KONG	3/18/1998	104079.6	1024640
JAPAN	3/18/1998	10-539987	
SINGAPORE	3/18/1998	9904590-8	68137
UNITED STATES	3/18/1998	09/155,248	6,472,376
UNITED STATES	8/20/2002	10/223,655	

ANTISENSE OLIGONUCLEOTIDE SEQUENCES AS INHIBITORS OF MICROORGANISMS

Country	Filed	Serial #	Patent #
CANADA	7/10/1998	2,294,305	2,294,305
UNITED STATES	7/9/1998	09/112,580	6,610,539

NEUROPILIN ANTISENSE OLIGONUCLEOTIDE SEQUENCES AND METHODS OF USING SAME TO MODULATE CELL GROWTH
(GTI-3611)

Country	Filed	Serial #	Patent #
AUSTRALIA	4/23/1999	34022/99	747639
MEXICO	4/23/1999	10277	
UNITED STATES	3/19/2002	09/298,264	7,087,580

OLIGONUCLEOTIDE SEQUENCES COMPLEMENTARY TO THIOREDOXIN OR THIOREDOXIN REDUCTASE GENES AND METHODS OF USING SAME TO MODULATE CELL GROWTH
(GTI-2601; GTI-3008)

Country	Filed	Serial #	Patent #
AUSTRALIA	1/29/1999	22612/99	760396
CHINA	1/29/1999	99802489.9	
MEXICO	1/29/1999	7455	
UNITED STATES	1/29/1999	09/601,144	6,568,514

INSULIN-LIKE GROWTH FACTOR II ANTISENSE OLIGONUCLEOTIDE SEQUENCES AND METHODS OF USING SAME TO MODULATE CELL GROWTH
(GTI-4006)

Country	Filed	Serial #	Patent #
AUSTRALIA	4/23/1999	34021/99	749802
CANADA	4/23/1999	2,328,825	
MEXICO	4/23/1999	10215	
UNITED STATES	4/22/1999	09/295,593	6,417,169

SMALL INTERFERING RNA MOLECULES AGAINST RIBONUCLEOTIDE REDUCTASE AND USES THEREOF
(siRNA)

Country	Filed	Serial #
CANADA	8/18/2005	2,577,036
EUROPE	8/18/2005	5774823.8
UNITED STATES	8/18/2005	11/573,879

PREPARATIONS OF ANTISENSE OLIGONUCLEOTIDES AGAINST THIOREDOXIN AND USES THEREOF
(GTI-2601/Sumitomo collaboration)

Country	Filed	Serial #
UNITED STATES	4/9/2007	60/910,689

Payment of fees and costs

Zur Kasse

Treasury and Accounts
D - 80298 Munchen
Fax: (+49-89) 2399-2528
(only for matters relating to accounts)

Please complete in typescript only

01 Name of payer: Gill Jennings & Every LLP

Payer's reference: LAS01886EP 20/07/07

Mode of payment:
- ☐ Bank/Giro transfer — Bank/Giro Office:
- ☐ Enclosed Cheque No.
- ☒ Debit from deposit account with the EPO is requested — Deposit account No.: 2805.0014

02 Address: Broadgate House, 7 Eldon Street, London EC2M 7LH UK.

Patent application / Patent No. (please use a separate form for each application)

03 EP 05706393.5 PCT PCT/CA05/00040 03

	Code		Currency	Amount
04	001	Filing fee		
05	002	Search fee		
06	005	Designation fee(s)		
07	015	Claims fee(s) (Rule 31 (1) EPC)		
08	055	Additional copy		
09	006	Examination fee		
10	007	Fee for grant including fee for printing (up to 35 pages)		
11	008	Additional fee for printing (more than 35 pages)		
12	033	Renewal fee for the 3rd year		
13	034	Renewal fee for the 4th year		
14	035	Renewal fee for the 5th year		
15	022	Registration of transfer	EUR	80.00
16				
17				
18				
19				
20				
21				
22		Total	EUR	80.00

Signature: Gill Jennings

Place, Date: London 18 JUL 2007

11 April 2007

European Patent Office
Erhardtstraße 27
80469 München
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European Trade Mark Attorneys

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www.gje.co.uk

Dear Sirs

European Patent Application No. 05706393.5
GeneSense Technologies Inc
Our Ref: LAS01886EP

In response to the communication dated 23 March 2007, a sequence listing on the prescribed data carrier is filed herewith. The information recorded on the data carrier is identical to the written sequence listing.

Yours faithfully
GILL JENNINGS & EVERY LLP

Elizabeth Flexer

JWJ/GJT/lmw

Filing Office Munich

File Number : 05706393.5

EPO - Munich
29
13. April 2007

Date of Receipt : .....

SEQL disc (EP)

EPO - Munich
29
13. April 2007

Sent on : .....

To : Karine Martin
(Munich - Room 2610)

BD/WP/NO/SE

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Europäisches Patentamt | European Patent Office | Office européen des brevets

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Broadgate House
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GRANDE BRETAGNE

EPO Customer Services
Tel.: +31 (0)70 340 45 00

Date: 23-03-2007

Reference	Application No./Patent No.
	05706393.5 - 2406 PCT/CA2005000040

Applicant/Proprietor: GeneSense Technologies Inc.

Formalities examination - Invitation to remedy deficiencies (Art. 91(2), R. 27a, 41(1) and 111(3) EPC)

The examination by the Receiving Section prescribed in Article 91(1)(b) and (d) EPC has revealed that the invention as disclosed in the above-mentioned European patent application contains nucleotides and/or amino acid sequences for which:

☐ no sequence listing has been submitted (R. 27a(1), 111(3) EPC);

☐ the sequence listing submitted does not comply with the rules laid down by the President of the European Patent Office in accordance with Rule 27a(1), Rule 111(3) EPC (cf. Decision of the President of the EPO dated 2 October 1998, published in Supplement No. 2 to Official Journal No. 11/1998) since

- ☐ one or more of the mandatory items is (are) not indicated in the sequence listing;
- ☐ not all the sequences disclosed in the application are included in the sequence listing;
- ☐ the sequence listing is not represented in accordance with WIPO standard ST.25;

☑ the sequence listing was not submitted on the prescribed data carrier (R. 27a(2), 111(3) EPC and the above-mentioned decision of the President);

☐ the statement that the information recorded on the data carrier is identical to the written sequence listing is missing (R. 27a(2) EPC);

☐ the data carrier is damaged and cannot be used;

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EPO Form 1128 06.00

YR50223

☐ Whereas the sequence listing was filed subsequently to the filing date, it is not accompanied by a statement that it does not include matter which goes beyond the content of the application as filed (R. 27a(3) EPC);

☑ see Annex

You are requested to remedy the deficiency within a

☑ period of **two months**

☐ non-extendable period of **one month**

after notification of this communication (R. 41(1) EPC and Art. 3 of the decision of the President).

If the specified deficiency is not remedied in due time, the European patent application will be refused (Art. 91(3) EPC).

We also draw your attention to the fact that any sequence listing submitted in response to this communication must be accompanied by a statement that it does not include matter which goes beyond the content of the application as filed and that the information recorded on the data carrier is identical to the written sequence listing.

Receiving Section

Europäisches Patentamt • European Patent Office • Office européen des brevets

Registered letter

Sequence Listing Department
P.B. 5818 - Patentlaan 2
2280 HV Rijswijk (ZH)
tel. +31 70 340 27 58 (direct)
fax +31 70 340 39 92 (direct)

Europäisches Patentamt	European Patent Office	Office Européen des Brevets
Eingangsstelle	Receiving Section	Section de dépôt

ANNEX

N.B.: The computer-readable form of the Sequence Listing was not furnished to the EPO.
The EPO hereby invites the applicant to submit a sequence listing, in computer-readable form, accompanied by the appropriate statement (Rule 27a(2) EPC).

We strongly recommend the applicant to use the **PatentIn** software to submit the sequence listing. For further details on how to obtain this software, see the remark below.

For further questions relating to the technical aspects of filing a sequence listing, please do not hesitate to contact Mr. Stéphane Nauche (tel.+31 70 340 2758).
To avoid any possible processing delay, please send sequence listing on paper and in computer-readable form (preferably in ASCII format) to the above address.

REMARK:
The latest version of PatentIn is available on our EPO website with following InterNet address:

www.european-patent-office.org/filingsoft/strand

Download is performed from that site, by following the download procedure. Please read carefully the information provided on that site.
The downloaded INSTALL.EXE file can be used for the installation of the new version from PatentIn. Once installed, W_UPATIN.EXE is the file to start PatentIn.

Tips with practical details about the use of PatentIn are available on that site as well.
If problems arise with the download of the PatentIn Software, a CD-ROM copy can be obtained through our Helpdesk via e-mail:

epoline@epo.org

For the download of the WIPO Standard ST.25, please activate the appropriate 'PDF' icon in the WIPO ST.25 paragraph. The Supplement No.2 to Official Journal No. 11/1998 can also be directly accessed at the following address:

www.european-patent-office.org/epo/pubs/oj98/11_98/11_s2_e.pdf

P.B.5818 - Patentlaan 2
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(070) 3 40 20 40
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Europäisches Patentamt	European Patent Office	Office européen des brevets
Generaldirektion 1	Directorate General 1	Direction générale 1

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Gill Jennings & Every LLP
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London EC2M 7LH
GRANDE BRETAGNE

EPO Customer Services
Tel.: +31 (0)70 340 45 00

Date
05.10.06

Reference	Application No./Patent No.
	05706393.5 - 2403 PCT/CA2005000040

Applicant/Proprietor
GeneSense Technologies Inc.

Notification of European publication number and information on the application of Article 67(3) EPC

The provisional protection under Article 67(1) and (2) EPC in the individual contracting states becomes effective only when the conditions referred to in Article 67(3) EPC have been fulfilled (for further details, see information brochure of the European Patent Office "National Law relating to the EPC" and additional information in the Official Journal of the European Patent Office).

Pursuant to Article 158(1) EPC the publication under Article 21 PCT of an international application for which the European Patent Office is a designated Office takes the place of the publication of a European patent application.

The bibliographic data of the above-mentioned Euro-PCT application will be published on 02.11.06 in Section I.1 of the European Patent Bulletin. The European publication number is 1715896.

In all future communications to the European Patent Office, please quote the application number plus Directorate number.

Receiving Section

Europäisches Patentamt • European Patent Office • Office européen des brevets

P.B.5818 - Patentlaan 2
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EPO Customer Services
Tel.: +31 (0)70 340 45 00

Date 01-09-2006

Reference	Application No./Patent No.
	05706393.5 - 2403 PCT/CA2005000040

Applicant/Proprietor
GeneSense Technologies Inc.

Communication pursuant to Rules 109 and 110 EPC

(1) Amendment of application documents, especially the claims (R. 109 EPC)

The above mentioned international (Euro-PCT) application has entered the European phase, or can do so, once the necessary conditions are fulfilled.

Under Articles 28, 41 PCT, Rules 52, 78 PCT and Rule 86(2) to (4) EPC, the applicant may amend the application documents after receiving the international search report.

Whether or not he has already done so, he now has a further opportunity to file amended claims or other application documents within a non-extendable time limit of one month after notification of the present communication (R. 109 EPC).

The claims applicable on expiry of the above time limit, i.e. those filed on entry into the European phase or in response to the present communication, will form the basis for the calculation of any claims fee to be paid (see page 2) and for any supplementary search to be carried out under Article 157(2) EPC (R. 109 EPC).

--2/

Registered letter
EPO Form 1226 01.02 EUCL

(2) Claims fees under Rule 110 EPC

If the application documents on which the European grant procedure is to be based comprise more than ten claims, a claims fee shall be payable for the eleventh and each subsequent claim within the period provided for in Rule 107(1) EPC.

☑ Based on the application documents currently on file, all necessary claims fees have already been paid (or the documents do not comprise more than 10 claims).

☐ All necessary fees will be/have been debited automatically according to the automatic debit order.

☐ The claims fee due for the claims ..... to ..... were not paid within the above-mentioned period.

Any non-paid claims fee, either based on the current set of claims or on any amended claims to be filed pursuant to Rule 109 EPC (see page 1), may still be validly paid within a non-extendable period of grace of **one month** after notification of this communication.

If a payment is made for only some of the claims, it must be indicated for which claims it is intended. If a claims fee is not paid in due time, the claim concerned is deemed to be abandoned (R. 110(4) EPC).

If claims fees have already been paid, but on expiry of the above-mentioned time limit there is a new set of claims containing fewer fee-incurring claims than previously, the claims fees in excess of those due under Rule 110(2), 2nd sentence, EPC will be refunded (R. 110(3) EPC).

You are reminded that any supplementary search under Article 157(2) EPC will relate only to the last set of claims applicable on expiry of the above time limit AND will be confined to those fee-incurring claims for which fees have been paid in due time.

The fee for the eleventh and each subsequent claim is EUR 45,00.

Receiving Section

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An das Europäische Patentamt | To the European Patent Office | A l'Office européen des brevets 1

EPO - Munich 67

09. Aug. 2006

Eintritt in die europäische Phase (EPA als Bestimmungsamt oder ausgewähltes Amt)

Entry into the European phase (EPO as designated or elected Office)

Entrée dans la phase européenne (l'OEB agissant en qualité d'office désigné ou élu)

Europäische Anmeldenummer oder, falls nicht bekannt, PCT-Aktenzeichen oder PCT-Veröffentlichungsnummer	European application number, or, if not known, PCT application or publication number	Numéro de dépôt de la demande de brevet européen ou, à défaut, numéro de dépôt PCT ou de publication PCT
	05706393.5 (PCT/CA 05/00040)	
Zeichen des Anmelders oder Vertreters (max. 15 Positionen)	Applicant's or representative's reference (max. 15 spaces)	Référence du demandeur ou du mandataire (15 caractères ou espaces au maximum)
	LAS01886EP	

1. Anmelder
Die Angaben über den (die) Anmelder sind in der internationalen Veröffentlichung enthalten oder vom Internationalen Büro nach der internationalen Veröffentlichung vermerkt worden.

☐ Änderungen, die das Internationale Büro noch nicht vermerkt hat, sind auf einem Zusatzblatt angegeben.

Zustellanschrift
(siehe Merkblatt II, 1)

1. Applicant
Indications concerning the applicant(s) are contained in the international publication or recorded by the International Bureau after the international publication.

Changes which have not yet been recorded by the International Bureau are set out on an additional sheet.

Address for correspondence
(see Notes II, 1)

1. Demandeur
Les indications concernant le(s) demandeur(s) figurent dans la publication internationale ou ont été enregistrées par le Bureau international après la publication internationale.

Les changements qui n'ont pas encore été enregistrés par le Bureau international sont indiqués sur une feuille additionnelle.

Adresse pour la correspondance
(voir notice II, 1)

2. Vertreter

Name (Nur einen Vertreter angeben, der in das europäische Patentregister eingetragen und an den zugestellt wird)

Geschäftsanschrift

Telefon

Telefax **Telex**

☐ Weitere(r) Vertreter auf Zusatzblatt

2. Representative

Name (Name **only one** representative who will be listed in the Register of European Patents and to whom notification will be made)

SAMUELS, Lucy Alice

Address of place of business
Gill Jennings & Every LLP
Broadgate House
7 Eldon Street
London EC2M 7LH

Telephone
020 7377-1377

Fax **Telex**
020 7377-1310

Additional representative(s) on additional sheet

2. Mandataire

Nom (N'indiquer **qu' un seul** mandataire, qui sera inscrit au Registre européen des brevets et auquel signification sera faite)

Adresse professionnelle

Téléphone

Téléfax **Télex**

Autre(s) mandataire(s) sur une feuille additionnelle

3. Vollmacht

☐ Einzelvollmacht ist beigefügt.

☐ Allgemeine Vollmacht ist registriert unter Nummer:

☐ Allgemeine Vollmacht ist eingereicht, aber noch nicht registriert.

☐ Die beim EPA als PCT-Anmeldeamt eingereichte Vollmacht schließt ausdrücklich die europäische Phase ein.

3. Authorisation

Individual authorisation is attached.

General authorisation has been registered under No:

A general authorisation has been filed, but not yet registered.

The authorisation filed with the EPO as PCT receiving Office expressly includes the European phase.

3. Pouvoir

Un pouvoir spécial est joint.

Un pouvoir général a été enregistré sous le n° :

Un pouvoir général a été déposé, mais n'est pas encore enregistré.

Le pouvoir général déposé à l'OEB agissant en qualité d'office récepteur au titre du PCT s'applique expressément à la phase européenne.

☒ **4. Prüfungsantrag**
Hiermit wird die Prüfung der Anmeldung gemäß Art. 94 EPÜ beantragt. Die Prüfungsgebühr wird (wurde) entrichtet.

Prüfungsantrag in einer zugelassenen Nichtamtssprache (siehe Merkblatt III, 5.2) :

4. Request for examination
Examination of the application under Art. 94 EPC is hereby requested. The examination fee is being (has been, will be) paid.

Request for examination in an admissible non-EPO language (see Notes III, 5.2) :

4. Requête en examen
Il est demandé que soit examinée la demande de brevet conformément à l'art. 94 CBE. Il est (a été, sera) procédé au paiement de la taxe d'examen.

Requête en examen dans une langue non officielle autorisée (voir notice III, 5.2) :

☒ **5. Abschriften**
Zusätzliche Abschrift(en) der im ergänzenden europäischen Recherchenbericht angeführten Schriftstücke wird (werden) beantragt.

Anzahl der **zusätzlichen** Sätze von Abschriften

5. Copies
Additional copy (copies) of the documents cited in the supplementary European search report is (are) requested.

Number of **additional** sets of copies

5. Copies
Prière de fournir une ou plusieurs copies supplémentaires des documents cités dans le rapport complémentaire de recherche européenne.

Nombre de jeux **supplémentaires** de copies

1

6. Für das Verfahren vor dem EPA bestimmte Unterlagen

6.1 Dem Verfahren vor dem EPA als **Bestimmungsamt** (PCT I) sind folgende Unterlagen zugrunde zu legen:

☒ die vom Internationalen Büro **veröffentlichten Anmeldungsunterlagen** (mit **allen** Ansprüchen, Beschreibung und Zeichnungen), gegebenenfalls mit den geänderten Ansprüchen nach Art. 19 PCT

☐ soweit sie nicht ersetzt werden durch die beigefügten **Änderungen.**

Falls nötig, sind Klarstellungen auf einem Zusatzblatt einzureichen!

6.2 Dem Verfahren vor dem EPA als **ausgewähltem Amt** (PCT II) sind folgende Unterlagen zugrunde zu legen:

☒ die dem **Internationalen vorläufigen Prüfungsbericht zugrunde gelegten Unterlagen,** einschließlich seiner eventuellen **Anlagen**
(Solche Anlagen müssen immer beigefügt werden)

☒ soweit sie nicht ersetzt werden durch die beigefügten **Änderungen.**

Falls nötig, sind Klarstellungen auf einem Zusatzblatt einzureichen!

☒ Sind dem EPA als mit der internationalen vorläufigen Prüfung beauftragten Behörde **Versuchsberichte** zugegangen, dürfen diese dem Verfahren vor dem EPA zugrunde gelegt werden.

6. Documents intended for proceedings before the EPO

6.1 Proceedings before the EPO as **designated Office** (PCT I) are to be based on the following documents:

the **application documents published** by the International Bureau (with **all** claims, description and drawings), where applicable with amended claims under Art. 19 PCT

unless replaced by the **amendments** enclosed.

Where necessary, clarifications must be submitted on a separate sheet!

6.2 Proceedings before the EPO as **elected Office** (PCT II) are to be based on the following documents:

the **documents on which the international preliminary examination report is based,** including its possible **annexes**
(Such annexes must always be filed)

unless replaced by the **amendments** enclosed.

Where necessary, clarifications must be submitted on a separate sheet!

If the EPO as International Preliminary Examining Authority has received **test reports,** these may be used as the basis of proceedings before the EPO.

6. Pièces destinées à la procédure devant l'OEB

6.1 La procédure devant l'OEB agissant en qualité **d'office désigné** (PCT I) doit se fonder sur les pièces suivantes :

les **pièces de la demande publiée** par le Bureau international (avec **toutes** les revendications, la description et les dessins), éventuellement avec les revendications modifiées conformément à l'article 19 du PCT

dans la mesure où elles ne sont pas remplacées par les **modifications** jointes.

Le cas échéant, des explications doivent être jointes sur une feuille additionnelle!

6.2 La procédure devant l'OEB **agissant en qualité d'office élu** (PCT II) doit se fonder sur les pièces suivantes :

les **pièces sur lesquelles se fonde le rapport d'examen préliminaire international,** y compris ses **annexes** éventuelles
(De telles annexes sont toujours à joindre)

dans la mesure où elles ne sont pas remplacées par les **modifications** jointes.

Le cas échéant, des explications doivent être jointes sur une feuille additionnelle!

Si l'OEB, agissant en qualité d'administration chargée de l'examen préliminaire international, a reçu des **rapports d'essais,** ceux-ci peuvent constituer la base de la procédure devant l'OEB.

	7. Übersetzungen Beigefügt sind die nachfolgend angekreuzten Übersetzungen in einer der Amtssprachen des EPA (Deutsch, Englisch, Französisch):	**7. Translations** Translations in one of the official languages of the EPO (English, French, German) are enclosed as crossed below:	**7. Traductions** Vous trouverez, ci-joint, les traductions cochées ci-après dans l'une des langues officielles de l'OEB (allemand, anglais, français) :
	• *Im Verfahren vor dem EPA als **Bestimmungsamt oder ausgewähltem Amt** (PCT I + II):*	• *In proceedings before the EPO as **designated or elected Office** (PCT I + II):*	• *Dans la procédure devant l'OEB agissant en qualité d'**office désigné ou élu** (PCT I + II):*
☐	Übersetzung der **ursprünglich eingereichten internationalen Anmeldung** (Beschreibung, Ansprüche, etwaige Textbestandteile in den Zeichnungen), der veröffentlichten Zusammenfassung, und etwaiger Angaben über biologisches Material nach Regel 13bis.3 und 13bis.4 PCT	Translation of the **international application** (description, claims, any text in the drawings) **as originally filed**, of the abstract as published and of any indication under Rule 13bis.3 and 13bis.4 PCT regarding biological material	Traduction de la **demande internationale telle que déposée initialement** (description, revendications, textes figurant éventuellement dans les dessins), de l'abrégé publié, et de toutes indications visées aux règles 13bis.3 et 13bis.4 du PCT concernant le matériel biologique
☐	Übersetzung der **prioritätsbegründenden Anmeldung(en)**	Translation of **the priority application(s)**	Traduction de la (des) **demande(s) ouvrant le droit de priorité**
☐	Es wird hiermit erklärt, daß die internationale Anmeldung in ihrer ursprünglich eingereichten Fassung eine vollständige Übersetzung der früheren Anmeldung ist (Regel 38(5) EPÜ)	It is hereby declared that the international application as originally filed is a complete translation of the previous application (Rule 38(5) EPC)	Il est déclaré par la présente que la demande internationale telle que déposée initialement est une traduction intégrale de la demande antérieure (règle 38(5) CBE)
	• ***Zusätzlich** im Verfahren vor dem EPA als **Bestimmungsamt** (PCT I):*	• ***In addition**, in proceedings before the EPO as **designated Office** (PCT I):*	• ***De plus**, dans la procédure devant l'OEB agissant en qualité d'**office désigné** (PCT I) :*
☐	Übersetzung der nach Art. 19 PCT **geänderten Ansprüche** nebst Erklärung, falls diese dem Verfahren vor dem EPA zugrunde gelegt werden sollen (siehe Feld 6)	Translation of **amended claims** and any statement under Art. 19 PCT, if the claims as amended are to form the basis for the proceedings before the EPO (see Section 6)	Traduction des **revendications modifiées** et de la déclaration faite conformément à l'article 19 du PCT, si la procédure devant l'OEB doit être fondée sur les revendications modifiées (voir la rubrique 6)
	• ***Zusätzlich** im Verfahren vor dem EPA als **ausgewähltem Amt** (PCT II):*	• ***In addition**, in proceedings before the EPO as **elected Office** (PCT II):*	• ***De plus**, dans la procédure devant l'OEB agissant en qualité d'**office élu** (PCT II) :*
☐	Übersetzung der **Anlagen zum internationalen vorläufigen Prüfungsbericht**	Translation of any **annexes to the international preliminary examination report**	Traduction des **annexes du rapport d'examen préliminaire international**
☐	**8. Biologisches Material** Die Erfindung bezieht sich auf bzw. verwendet biologisches Material, das nach Regel 28 EPÜ hinterlegt worden ist.	**8. Biological material** The invention relates to and/or uses biological material deposited under Rule 28 EPC.	**8. Matière biologique** L'invention concerne et/ou utilise de la matière biologique, déposée conformément à la règle 28 CBE.
☐	Die **Angaben nach Regel 28(1)c) EPÜ** (falls noch nicht bekannt, die Hinterlegungsstelle und das (die) Bezugszeichen [Nummer, Symbole usw.] des Hinterlegers) sind in der internationalen Veröffentlichung oder in der gemäß Feld 7 eingereichten Übersetzung enthalten auf:	The **particulars referred to in Rule 28(1)(c) EPC** (if not yet known, the depository institution and the identification reference(s) [number, symbols etc.] of the depositor) are given in the international publication or in the translation submitted under Section 7 on:	Les **indications visées à la règle 28(1)c) CBE** (si non encore connues, l'autorité de dépôt et la (les) référence(s) d'identification [numéro ou symboles etc.] du déposant) figurent dans la publication internationale ou dans une traduction produite conformément à la rubrique 7 à la / aux:
	Seite(n) / Zeile(n)	page(s) / line(s)	page(s) / ligne(s)
	Die **Empfangsbescheinigung(en)** der Hinterlegungsstelle	The **receipt(s) of deposit** issued by the depositary institution	Le(s) **récépissé(s) de dépôt** délivré(s) par l'autorité de dépôt
☐	ist (sind) beigefügt	is (are) enclosed	est (sont) joint(s)
☐	wird (werden) nachgereicht	will be filed at a later date	sera (seront) produit(s) ultérieurement
☐	Verzicht auf die Verpflichtung des Antragstellers nach Regel 28(3) EPÜ auf gesondertem Schriftstück	Waiver of the right to an undertaking from the requester pursuant to Rule 28(3) EPC attached.	Renonciation, sur document distinct, à l'engagement du requérant au titre de la règle 28(3) CBE.

9. Nucleotid- und Aminosäuresequenzen

☐ Die nach Regeln 5.2 und 13ter PCT sowie Regel 111(3) EPÜ erforderlichen Unterlagen liegen dem EPA bereits vor.

☒ Das schriftliche Sequenzprotokoll wird anliegend nachgereicht.

☒ Das Sequenzprotokoll geht nicht über den Inhalt der Anmeldung in der ursprünglich eingereichten Fassung hinaus.

☐ Der vorgeschriebene Datenträger ist beigefügt.

☐ Die auf dem Datenträger gespeicherte Information stimmt mit dem schriftlichen Sequenzprotokoll überein.

9. Nucleotide and amino acid sequences

The items necessary in accordance with Rules 5.2 and 13ter PCT and Rule 111(3) EPC have already been furnished to the EPO.

The written sequence listing is furnished herewith.

The sequence listing does not include matter which goes beyond the content of the application as filed.

The prescribed data carrier is enclosed.

The information recorded on the data carrier is identical to the written sequence listing.

9. Séquences de nucléotides et d'acides aminés

Les pièces requises selon les règles 5.2 et 13ter PCT et la règle 111(3) CBE ont déjà été déposées auprès de l'OEB.

La liste de séquences écrite est produite ci-joint.

La liste de séquences ne contient pas d'éléments s'étendant au-delà du contenu de la demande telle qu'elle a été déposée.

Le support de données prescrit est joint.

L'information figurant sur le support de données est identique à celle que contient la liste de séquences écrite.

10. Benennungsgebühren

☒ 10.1 Es ist derzeit beabsichtigt, den **siebenfachen** Betrag einer Benennungsgebühr zu entrichten. Damit gelten die Benennungsgebühren für **alle Vertragsstaaten des EPÜ**[1] als entrichtet (Art. 2 Nr. 3 GebO), soweit sie **in der internationalen Anmeldung** bestimmt sind[2].

☐ 10.2 Abweichend von der Erklärung in Nr. 10.1 ist derzeit beabsichtigt, **weniger als sieben** Benennungsgebühren für folgende **in der internationalen Anmeldung bestimmte Vertragsstaaten des EPÜ**[2] zu entrichten:

(1) ☐ _____ (4) ☐ _____

(2) ☐ _____ (5) ☐ _____

(3) ☐ _____ (6) ☐ _____

Soweit unter Nr. 10.2 Vertragsstaaten aufgeführt sind, wird beantragt, für die dort nicht aufgeführten Vertragsstaaten von der Zustellung einer Mitteilung nach Regel 108(3) EPÜ abzusehen.

☒ 10.3 Wird ein **automatischer Abbuchungsauftrag** erteilt (Feld 12), so wird das EPA beauftragt, bei Ablauf der Grundfrist nach Regel 107 (1)d) EPÜ den siebenfachen Betrag einer Benennungsgebühr abzubuchen. Ist eine Erklärung nach Nr. 10.2 abgegeben worden, so sollen die Benennungsgebühren nur für die dort angegebenen Vertragsstaaten abgebucht werden, sofern dem EPA nicht bis zum Ablauf der Grundfrist ein anderslautender Auftrag zugeht.

10. Designation fees

10.1 It is currently intended to pay **seven times** the amount of the designation fee. The designation fees for **all the EPC contracting states**[1] **designated in the international application**[2] are thereby deemed to have been paid (Art. 2 No. 3 RFees).

10.2 The declaration in No. 10.1 does not apply. Instead, it is currently intended to pay **fewer than seven** designation fees for the following **EPC contracting states**[2] **designated in the international application**:

If contracting states are indicated under No. 10.2, it is requested that no communication under Rule 108(3) EPC be issued for contracting states not thus indicated.

10.3 If an **automatic debit order** has been issued (Section 12), the EPO is authorised, on expiry of the basic period under Rule 107(1)(d) EPC, to debit seven times the amount of the designation fee. If states are indicated under No. 10.2, the EPO will debit designation fees only for those states, unless instructed otherwise before the basic period expires.

10. Taxes de désignation

10.1 Il est actuellement envisagé de payer un montant correspondant à **sept fois** la taxe de désignation. Les taxes de désignation sont ainsi réputées payées pour **tous les Etats contractants de la CBE**[1] **désignés dans la demande internationale**[2] (art. 2, point 3 du RRT).

10.2 Contrairement à ce qui est indiqué au n° 10.1, il est actuellement envisagé de payer **moins de sept** taxes de désignation pour les **Etats contractants de la CBE**[2] suivants **désignés dans la demande internationale** :

Si des Etats contractants sont mentionnés au n° 10.2, prière de ne pas procéder à la signification d'une notification prévue par la règle 108(3) CBE pour les Etats contractants n'y étant pas mentionnés.

10.3 Si un **ordre de prélèvement automatique** est donné (rubrique 12), il est demandé à l'OEB de prélever, à l'expiration du délai normal visé à la règle 107(1)d) CBE, un montant correspondant à sept fois la taxe de désignation. Si une déclaration a été faite au n° 10.2, les taxes de désignation ne sont à prélever que pour les Etats contractants qui y sont indiqués, sauf instruction contraire reçue par l'OEB avant l'expiration du délai normal.

1 Stand bei Drucklegung: 27 Vertragsstaaten, und zwar: / Status when this form was printed: 27 contracting states, namely / Situation à la date d'impression : 27 Etats contractants, à savoir : **AT** Österreich / Austria / Autriche, **BE** Belgien / Belgium / Belgique, **BG** Bulgarien / Bulgaria / Bulgarie, **CH / LI** Schweiz und Liechtenstein / Switzerland and Liechtenstein / Suisse et Liechtenstein, **CY** Zypern / Cyprus / Chypre, **CZ** Tschechische Republik / Czech Republic / République tchèque, **DE** Deutschland / Germany / Allemagne, **DK** Dänemark / Denmark / Danemark, **EE** Estland / Estonia / Estonie, **ES** Spanien / Spain / Espagne, **FI** Finnland / Finland / Finlande, **FR** Frankreich / France / France, **GB** Vereinigtes Königreich / United Kingdom / Royaume-Uni, **GR** Griechenland / Greece / Grèce, **HU** Ungarn / Hungary / Hongrie, **IE** Irland / Ireland / Irlande, **IT** Italien / Italy / Italie, **LU** Luxemburg / Luxembourg / Luxembourg, **MC** Monaco / Monaco / Monaco, **NL** Niederlande / Netherlands / Pays-Bas, **PT** Portugal / Portugal / Portugal, **RO** Rumänien / Romania / Roumanie, **SE** Schweden / Sweden / Suède, **SI** Slowenien / Slovenia / Slovénie, **SK** Slowakische Republik / Slovak Republic / République slovaque, **TR** Türkei / Turkey / Turquie

2 Für folgende Staaten nur möglich, falls in der internationalen Anmeldung am oder nach folgendem Tag bestimmt: Slowakische Republik, Bulgarien, Tschechische Republik und Estland: 1. Juli 2002, Slowenien: 1. Dezember 2002, Ungarn: 1. Januar 2003 und Rumänien: 1. März 2003. / For the following states this is possible only if they are designated in the international application on or after the stated date: Slovak Republic, Bulgaria, Czech Republic and Estonia: 1 July 2002, Slovenia: 1 December 2002, Hungary: 1 January 2003 and Romania: 1 March 2003. / En ce qui concerne les Etats suivants seulement si la désignation a été effectuée dans la demande internationale à la date suivante ou à une date ultérieure: République slovaque, Bulgarie, République tchèque et Estonie: 1er juillet 2002, Slovénie: 1er décembre 2002, Hongrie: 1er janvier 2003 et Roumanie: 1er mars 2003.

☒ **11. Erstreckung des europäischen Patents**
Bei Zahlung der Erstreckungsgebühr(en) gilt diese Anmeldung auch als wirksamer Erstreckungsantrag für die in der internationalen Anmeldung bestimmten »Erstreckungsstaaten«. Es ist beabsichtigt, diese Gebühr(en) für folgende Staaten zu entrichten:

11. Extension of the European patent
On payment of the extension fee(s) this application is also deemed to be a request for extension to all the "extension states" designated in the international application. It is intended to pay the fee(s) for the following states:

11. Extension des effets du brevet européen
La taxe (Les taxes) d'extension payée(s), la présente demande est également réputée être une demande d'extension à tous les «Etats autorisant l'extension» désignés dans la demande internationale. Il est envisagé de payer la taxe (les taxes) d'extension pour les Etats suivants:

☐	SI	Slowenien [1]	Slovenia [1]	Slovénie [1]
☐	LT	Litauen	Lithuania	Lituanie
☐	LV	Lettland	Latvia	Lettonie
☐	AL	Albanien	Albania	Albanie
☐	RO	Rumänien [1]	Romania [1]	Roumanie [1]
☐	MK	Ehemalige jugoslawische Republik Mazedonien	Former Yugoslav Republic of Macedonia	Ex-République yougoslave de Macédoine
☐	____	_____ [2]	_____ [2]	_____ [2]

1) Für Slowenien und Rumänien nur möglich, falls in der internationalen Anmeldung bis 30. November 2002 (Slowenien) oder bis 28. Februar 2003 (Rumänien) bestimmt. / For Slovenia and Romania this is possible only if they are designated in the international application up to 30 November 2002 (Slovenia) or 28 February 2003 (Romania). / En ce qui concerne la Slovénie et la Roumanie, seulement si la désignation a été effectuée dans la demande internationale jusqu'au 30 novembre 2002 (Slovénie) ou jusqu'au 28 février 2003 (Roumanie).

2) Platz für Staaten, mit denen »Erstreckungsabkommen« nach Drucklegung dieses Formblatts in Kraft treten und die in der internationalen Anmeldung bestimmt waren. / Space for States with which "extension agreements" enter into force after this form has been printed and which were designated in the international application. / Prévu pour des Etats à l'égard desquels des «accords d'extension» entreront en vigueur après l'impression du présent formulaire et qui ont été désignés dans la demande internationale.

12. Automatischer Abbuchungsauftrag ***(Nur möglich für Inhaber von beim EPA geführten laufenden Konten)***

☐ Das EPA wird beauftragt, nach Maßgabe der Vorschriften über das automatische Abbuchungsverfahren fällige Gebühren und Auslagen vom untenstehenden laufenden Konto abzubuchen. In Bezug auf die **Benennungsgebühren** wird auf Feld 10.3 verwiesen. Das EPA wird ferner beauftragt, die **Erstreckungsgebühren** für jeden in Feld 11 angekreuzten »Erstreckungsstaat« bei Ablauf der Grundfrist zu ihrer Zahlung abzubuchen, sofern ihm nicht bis dahin ein anderslautender Auftrag zugeht.

Nummer und Kontoinhaber

12. Automatic debit order ***(for EPO deposit account holders only)***

The EPO is hereby authorised, under the Arrangements for the automatic debiting procedure, to debit from the deposit account below any fees and costs falling due. For **designation fees**, see Section 10.3. The EPO is also authorised, on expiry of the basic period for paying the **extension fees**, to debit those fees for each of the "extension states" marked with a cross in Section 11, unless instructed otherwise before the said period expires.

Number and account holder

12. Ordre de prélèvement automatique ***(uniquement possible pour les titulaires de comptes courants ouverts auprès de l'OEB)***

Par la présente, il est demandé à l'OEB de prélever du compte courant ci-dessous les taxes et frais venant à échéance, conformément à la réglementation relative au prélèvement automatique. Pour les **taxes de désignation,** se reporter à la rubrique 10.3. Il est en outre demandé à l'OEB de prélever, à l'expiration du délai normal prévu pour leur paiement, les **taxes d'extension** pour chaque «Etat autorisant l'extension» coché à la rubrique 11, sauf instruction contraire reçue avant l'expiration de ce délai.

Numéro et titulaire du compte

☒ **13.** Eventuelle **Rückzahlungen** auf das beim EPA geführte laufende Konto

Nummer und Kontoinhaber

13. Any **reimbursement** to EPO deposit account
Gill Jennings & Every LLP
Number and account holder
2805.0014

13. Remboursements éventuels à effectuer sur le compte courant ouvert auprès de l'OEB
Numéro et titulaire du compte

14. Unterschrift(en) des (der) Anmelder(s) oder Vertreters

Ort / Datum

Für Angestellte (Art. 133(3) EPÜ) mit allgemeiner Vollmacht:

Nr.

Name(n) des (der) Unterzeichneten bitte in Druckschrift wiederholen. Bei juristischen Personen bitte auch die Stellung des (der) Unterzeichneten innerhalb der Gesellschaft in Druckschrift angeben.

14. Signature(s) of applicant(s) or representative

SAMUELS, Lucy Alice

Place / Date London/7 August 2006

For employees (Art. 133(3) EPC) having a general authorisation:

No.

Please print name(s) under signature(s). In the case of legal persons, the position of the signatory within the company should also be printed.

14. Signature(s) du (des) demandeur(s) ou du mandataire

Lieu / Date

Pour les employés (art. 133(3) CBE) disposant d'un pouvoir général :

N°

Le ou les noms des signataires doivent être indiqués en caractères d'imprimerie. S'il s'agit d'une personne morale, la position occupée au sein de celle-ci par le ou les signataires doit également être indiquée en caractères d'imprimerie.

SEQUENCE LISTING

<110> GeneSense Technologies Inc. et al.

<120> Antisense Oligonucleotides Directed To Ribonucleotide Reductase R2 and Uses Thereof in Combination Therapies for the Treatment of Cancer

<130> 683-134pct

<140> n/a
<141> 2005-01-12

<150> US60/535,496
<151> 2004-01-12

<150> US60/602,817
<151> 2004-08-18

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<220>
<223> Control antisense oligonucleotide

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complementary to human ribonucleotide reductase R2 mRNA

<400> 7
tgcctccgac ccttccca 18

<210> 8
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Partially Phosphorothioated AS-II-75-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 8
cgcgcgctcc cggcccttcc 20

<210> 9
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-75-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 9
cgcgcgctcc cggcccttcc 20

<210> 10
<211> 14
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-79-14 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 10
cgcgctcccg gccc 14

<210> 11
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-109-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 11
cccctcactc cagcagcctt 20

<210> 12
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-110-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 12
acccctcact ccagcagcct 20

<210> 13
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-114-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 13
ggcgacccct cactccagca 20

<210> 14
<211> 12
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-127-12 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 14
gcacgggcga cc 12

<210> 15
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-130-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 15
tgggacaggg tgcacgggcg 20

<210> 16
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-134-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 16
gacggctggg acagggtgca 20

<210> 17
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-151-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 17
gagcagccag gacaggacgg 20

<210> 18
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-163-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 18
gcgaagcaga gcgagcagcc 20

<210> 19
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-166-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 19
gcagcgaagc agagcgagca 20

<210> 20
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-185-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 20
gggagagcat agtggaggcg 20

<210> 21
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-189-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 21
cggagggaga gcatagtgga 20

<210> 22
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-201-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 22
gcgagcggga cacggaggga 20

<210> 23
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-217-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 23
cgggtccgtg atgggcgcga 20

<210> 24
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-225-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 24
agctgctgcg ggtccgtgat 20

<210> 25
<211> 14
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-253-14 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 25
cccgttcagc ggcg 14

<210> 26
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-280-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 26
cggcggcgtg ttctccttgt 20

<210> 27
<211> 12
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-288-12 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 27
cggcggcgtg tt 12

<210> 28
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-323-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 28
tcctcgcggt cttgctggcc 20

<210> 29
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-344-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 29
ccgtgggctc ctggaagatc 20

<210> 30
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-362-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 30
ctgctttagt tttcggctcc 20

<210> 31
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-391-17 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 31
cggctcatcc tccacgc 17

<210> 32
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-404-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 32
ggttttctct cagcagcggc 20

<210> 33
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-412-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 33
gcggcggggg ttttctctca 20

<210> 34
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-414-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 34
aagcggcggg ggttttctct 20

<210> 35
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-425-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 35
ggaagatgac aaagcggcgg 20

<210> 36
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-439-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 36
atggtactcg atggggaaga 20

<210> 37
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-472-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 37
agcctctgcc ttcttataca 20

<210> 38
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-494-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 38
cctcctcggc ggtccaaaag 20

<210> 39
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-496-16 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 39
tcctcggcgg tccaaa 16

<210> 40
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-549-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 40
tatctctcct cgggtttcag 20

<210> 41
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-579-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 41
gcaaagaaag ccagaacatg 20

<210> 42
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-619-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 42
tcgctccacc aagttttcat 20

<210> 43
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-634-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 43
aacttcttgg ctaaatcgct 20

<210> 44
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-667-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 44
gaagccatag aaacagcggg 20

<210> 45
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-784-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 45
gacacaaggc atcgtttcaa 20

<210> 46
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-798-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 46
tctgccttct tcttgacaca 20

<210> 47
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-816-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 47
atccagcgca aggcccagtc 20

<210> 48
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-861-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 48
gcaaaggcta caacacgttc 20

<210> 49
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-890-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 49
aaccggaaaa gaaaatgcct 20

<210> 50
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-909-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 50
ggcatcagtc ctcgtttctt 20

<210> 51
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-933-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 51
ggcatcagtc ctcgtttctt 20

<210> 52
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-981-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 52
tgtaaaccct catctctgct 20

<210> 53
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1001-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 53
tcaggcaagc aaaatcacag 20

<210> 54
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1006-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 54
gaacatcagg caagcaaaat 20

<210> 55
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1023-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 55
ttgtgtacca ggtgtttgaa 20

<210> 56
<211> 20
<212> DNA
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<220>
<223> AS-II-1040-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 56
ctctctcctc cgatggtttg 20

<210> 57
<211> 20
<212> DNA
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<220>
<223> AS-II-1048-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 57
ttctcttact ctctcctccg 20

<210> 58
<211> 20
<212> DNA
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<220>
<223> AS-II-1144-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 58
gtattgcttc attagagtgc 20

<210> 59
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1182-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 59
cccagttcca gcataagtct 20

<210> 60
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1197-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 60
aaaaccttgc taaaacccag 20

<210> 61
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1217-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 61
caaatgggtt ctctactctg 20

<210> 62
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1224-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 62
ataaagtcaa atgggttctc 20

<210> 63
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1254-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 63
ttagtctttc cttccagtga 20

<210> 64
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1278-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 64
tcgcctactc tcttctcaaa 20

<210> 65
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1288-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 65
cctctgatac tcgcctactc 20

<210> 66
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1302-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 66
gacatcactc ccatcctctg 20

<210> 67
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1335-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 67
gcatccaagg taaaagaatt 20

<210> 68
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1338-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 68
tcagcatcca aggtaaaaga 20

<210> 69
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1342-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 69
gaagtcagca tccaaggtaa 20

<210> 70
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1345-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 70
ttagaagtca gcatccaagg 20

<210> 71
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1362-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 71
gcacatcttc agttcattta 20

<210> 72
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1364-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 72
gggcacatct tcagttcatt 20

<210> 73
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1381-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 73
aaaaatcagc caagtaaggg 20

<210> 74
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1390-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 74
atggaaaaaa aaaatcagcc 20

<210> 75
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1438-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 75
ttcatggtgt ggctagttgg 20

<210> 76
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1499-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 76
aggactggtt gtgaggtagc 20

<210> 77
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1517-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 77
ccagcactat aaacagacag 20

<210> 78
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1538-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 78
ttctggcaaa aggtgatact 20

<210> 79
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1560-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 79
gtaagtcaca gccagccagg 20

<210> 80
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1581-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 80
actgccattg tcactgctat 20

<210> 81
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1659-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 81
tggctgtgct ggttaaagga 20

<210> 82
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1666-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 82
ttttaactgg ctgtgctggt 20

<210> 83
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1700-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 83
attaaaatct gcgttgaagc 20

<210> 84
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1768-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 84
tatcgccgcc gtgagtacaa 20

<210> 85
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1773-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 85
gctattatcg ccgccgtgag 20

<210> 86
<211> 12
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1775-12 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 86
atcgccgccg tg 12

<210> 87
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1790-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 87
gaaaccaaat aaatcaagct 20

<210> 88
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1819-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 88
ttagtggtca ggagaatgta 20

<210> 89
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1976-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 89
tggcaccaac tgactaatat 20

<210> 90
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-1989-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 90
cctgtcttct atctggcacc 20

<210> 91
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2009-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 91
gccacaggat aaaaacacaa 20

<210> 92
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2026-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 92
cccaggacac tacacaagcc 20

<210> 93
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2044-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 93
tcagaggggg cagagaatcc 20

<210> 94
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2067-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 94
tcctttatcc cacaacactc 20

<210> 95
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2083-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 95
ccttgccctg agagattcct 20

<210> 96
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Partially Phosphorothioated AS-II-2083-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 96
ccttgccctg agagattcct 20

<210> 97
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2128-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 97
ggcccagatc acccctaaat 20

<210> 98
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2151-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 98
aaacggcttc tcacacatat 20

<210> 99
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2164-20 antisense oligonucleotides

complementary to human ribonucleotide reductase R2 mRNA

<400> 99
gagaaataaa atgaaacggc 20

<210> 100
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2182-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 100
cgttgaggaa aatacagtga 20

<210> 101
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2229A-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 101
gctcccacat atgaaaactc 20

<210> 102
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> AS-II-2372-20 antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 102
cacacaacct acttacacca 20

<210> 103
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Antisense oligonucleotides complementary to human

ribonucleotide reductase R2 mRNA

<400> 103
tcctggaaga tcctcctcgc 20

<210> 104
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Antisense oligonucleotides complementary to human ribonucleotide reductase R2 mRNA

<400> 104
tcccacatat gagaaaactc 20

<210> 105
<211> 2500
<212> DNA
<213> Homo sapiens

<220>
<221> mRNA
<222> (1)...(2500)
<223> ribonucleotide reductase R2 mRNA

<400> 105
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gtgaggggtc gcccgtgcac cctgtcccag ccgtcctgtc ctggctgctc gctctgcttc 180
gctgcgcctc cactatgctc tccctccgtg tcccgctcgc gcccatcacg gacccgcagc 240
agctgcagct ctcgccgctg aaggggctca gcttggtcga caaggagaac acgccgccgg 300
ccctgagcgg gacccgcgtc ctggccagca agaccgcgag gaggatcttc caggagccca 360
cggagccgaa aactaaagca gctgcccccg gcgtggagga tgagccgctg ctgagagaaa 420
acccccgccg ctttgtcatc ttccccatcg agtaccatga tatctggcag atgtataaga 480
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gggaatccct gaaacccgag gagagatatt ttatatccca tgttctggct ttctttgcag 600
caagcgatgg catagtaaat gaaaacttgg tggagcgatt tagccaagaa gttcagatta 660
cagaagcccg ctgtttctat ggcttccaaa ttgccatgga aaacatacat tctgaaatgt 720
atagtcttct tattgacact tacataaaag atcccaaaga aagggaattt ctcttcaatg 780
ccattgaaac gatgccttgt gtcaagaaga aggcagactg ggccttgcgc tggattgggg 840
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ttacctgtag ttcataaaaa aaaaaaaaaa aaaaaaaaaa 2500

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A combination product for use in the treatment of cancer in a mammal, said combination product comprising: an antisense oligonucleotide of between 7 and 100 nucleotides in length comprising at least 7 consecutive nucleotides complementary to a mammalian ribonucleotide reductase R2 subunit mRNA and one or more immunotherapeutic agents.

2. The combination product according to claim 1, wherein said mammalian ribonucleotide reductase R2 subunit mRNA is a human ribonucleotide reductase R2 subunit mRNA.

3. The combination product according to claim 2, wherein said human ribonucleotide reductase R2 subunit mRNA has a sequence as set forth in SEQ ID NO:105.

4. The combination product according to claim 2, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in any one of SEQ ID NOs:1 and 4-104.

5. The combination product according to according to claim 2, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in SEQ ID NO:1.

6. The combination product according to any one of claims 1 to 5, wherein said antisense oligonucleotide comprises one or more phosphorothioate internucleotide linkages.

7. The combination product according to any one of claims 1 to 6, wherein said cancer is an advanced cancer.

8. The combination product according to any one of claims 1 to 7, wherein said cancer is a metastatic cancer.

9. The combination product according to any one of claims 1 to 8, wherein said treatment is a first-line systemic therapy.

10. The combination product according to any one of claims 1 to 9, wherein said one or more immunotherapeutic agents are non-specific immunotherapeutic agents.

11. The combination product according to any one of claims 1 to 9, wherein said one or more immunotherapeutic agents are specific immunotherapeutic agents.

12. The combination product according to any one of claims 1 to 10, wherein said one or more immunotherapeutic agents are selected from the group of: a cytokine, a non-cytokine adjuvant, a monoclonal antibody and a cancer vaccine.

13. The combination product according to any one of claims 1 to 10, wherein said one or more immunotherapeutic agents are selected from the group of: a cytokine and a non-cytokine adjuvant.

14. The combination product according to any one of claims 1 to 10, wherein said one or more immunotherapeutic agents are one or more cytokines.

15. The combination product according to any one of claims 1 to 14, wherein said combination product further comprises one or more chemotherapeutic agents.

16. The combination product according to any one of claims 1 to 15, wherein said cancer is a solid cancer.

17. The combination product according to any one of claims 1 to 16, wherein said mammal is a human.

~~18. A method of treating cancer in a mammal comprising administering to said~~ mammal a combination product comprising:

(a) an antisense oligonucleotide of between 7 and 100 nucleotides in length comprising at least 7 consecutive nucleotides complementary to a mammalian ribonucleotide reductase R2 subunit mRNA, and

(b) one or more immunotherapeutic agents.

19. The method according to claim 18, wherein said mammalian ribonucleotide reductase R2 subunit mRNA is a human ribonucleotide reductase R2 subunit mRNA.

20. The combination product according to claim 19, wherein said human ribonucleotide reductase R2 subunit mRNA has a sequence as set forth in SEQ ID NO:105.

21. The method according to claim 19, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in any one of SEQ ID NOs:1 and 4-104.

22. The method according to according to claim 19, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in SEQ ID NO:1.

23. The method according to any one of claims 18 to 22, wherein said antisense oligonucleotide comprises one or more phosphorothioate internucleotide linkages.

24. The method according to any one of claims 18 to 23, wherein said cancer is an advanced cancer.

25. The method according to any one of claims 18 to 24, wherein said cancer is a metastatic cancer.

26. The method according to any one of claims 18 to 25, wherein said combination product is administered to said mammal as first-line systemic therapy.

27. The method according to any one of claims 18 to 26, wherein said one or more immunotherapeutic agents are non-specific immunotherapeutic agents.

28. The method according to any one of claims 18 to 26, wherein said one or more immunotherapeutic agents are specific immunotherapeutic agents.

29. The method according to any one of claims 18 to 27, wherein said one or more immunotherapeutic agents are selected from the group of: a cytokine, a non-cytokine adjuvant, a monoclonal antibody and a cancer vaccine.

30. The method according to any one of claims 18 to 27, wherein said one or more immunotherapeutic agents are selected from the group of: a cytokine and a non-cytokine adjuvant.

~~31. The method according to any one of claims 18 to 27, wherein said one or more~~ immunotherapeutic agents are one or more cytokines.

32. The method according to any one of claims 18 to 31, wherein said combination product further comprises one or more chemotherapeutic agents.

33. The method according to any one of claims 18 to 32, wherein said cancer is a solid cancer.

34. The method according to any one of claims 18 to 33, wherein said mammal is a human.

18 ~~35~~. Use of an antisense oligonucleotide of between 7 and 100 nucleotides in length comprising at least 7 consecutive nucleotides complementary to a mammalian ribonucleotide reductase R2 subunit mRNA and one or more immunotherapeutic agents in the manufacture of a medicament for the treatment of cancer in a mammal.

19 ~~36~~. The use according to claim 18, ~~35, wherein said mammalian ribonucleotide reductase~~ additionally comprising any of the features of claims 2 to 17. R2 subunit mRNA is a human ribonucleotide reductase R2 subunit mRNA.

37. The use according to claim 36, wherein said human ribonucleotide reductase R2 subunit mRNA has a sequence as set forth in SEQ ID NO:105.

38. The use according to claim 36, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in any one of SEQ ID NOs:1 and 4-104.

39. The use according to claim 36, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in SEQ ID NO:1.

40. The use according to any one of claims 35 to 39, wherein said antisense oligonucleotide comprises one or more phosphorothioate internucleotide linkages.

41. The use according to any one of claims 35 to 40, wherein said cancer is an advanced cancer.

~~42. The use according to any one of claims 35 to 41, wherein said cancer is a~~ metastatic cancer.

43. The use according to any one of claims 35 to 42, wherein said treatment is a first-line systemic therapy.

44. The use according to any one of claims 35 to 43, wherein said one or more immunotherapeutic agents are non-specific immunotherapeutic agents.

45. The use according to any one of claims 35 to 43, wherein said one or more immunotherapeutic agents are specific immunotherapeutic agents.

46. The use according to any one of claims 35 to 44, wherein said one or more immunotherapeutic agents are selected from the group of: a cytokine, a non-cytokine adjuvant, a monoclonal antibody and a cancer vaccine.

47. The use according to any one of claims 35 to 44, wherein said one or more immunotherapeutic agents are selected from the group of: a cytokine and a non-cytokine adjuvant.

48. The use according to any one of claims 35 to 44, wherein said one or more immunotherapeutic agents are one or more cytokines.

49. The use according to any one of claims 35 to 48, wherein said combination product further comprises one or more chemotherapeutic agents.

50. The use according to any one of claims 35 to 49, wherein said cancer is a solid cancer.

51. The use according to any one of claims 35 to 50, wherein said mammal is a human.

20 ~~52~~. A pharmaceutical kit comprising a combination product for the treatment of cancer, said combination product comprising:

(a) an antisense oligonucleotide of between 7 and 100 nucleotides in length comprising at least 7 consecutive nucleotides complementary to a mammalian ribonucleotide reductase R2 subunit mRNA, and

(b) one or more immunotherapeutic agents.

21 ~~53~~. A combination product for use in the treatment of renal cancer in a subject, said combination product comprising: an antisense oligonucleotide of between 7 and 100 nucleotides in length comprising at least 7 consecutive nucleotides complementary to SEQ ID NO:1 and one or more cytokines.

22 ~~54~~. The combination product according to claim 21 ~~53~~, wherein said one or more cytokines are selected from: interferon alpha and interleukin-2.

23 ~~55~~. The combination product according to claim 21 ~~53~~ or 22 ~~54~~, wherein said treatment is a first-line systemic therapy.